

REMARKS

Applicants respectfully request entry of the foregoing and reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks which follow.

Claims 1-15 are pending in the application, Claims 16 and 17 having been canceled above.

By the foregoing amendments, Applicants have amended Claims 1-4 and 7-15 to address § 112 issues, correct various informalities, and place the claims into a more conventional U.S. patent format. A claim that has not been amended in a manner that narrows the scope of the claim, should be accorded its full range of equivalents.

Turning now to the Official Action, Claims 1-17 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. For at least the reasons that follow, withdrawal of the rejection is in order.

Concerning the rejection of Claim 1, Applicants have amended the preamble to read “an improved process for isolation of withaferin-A from plant materials, said process comprising the steps of,” as suggested by the Examiner. Applicants further amended Claim 1 in response to the issues with step (i) so that step (i) reads “extracting the plant materials in an aqueous alcohol extraction solvent.”

Applicants further amended Claim 1 to address the issues raised with respect to step (ii) so that step (ii) reads, in part, “followed by chromatographic separation to obtain a withanolide preparation.”

Applicants further amended Claim 1 so that step (iii) reads, "portioning out withanolide aglycones from the withanolide preparation, as obtained in step (ii), into chloroform followed by evaporation of said chloroform to obtain a chloroform extract."

Finally, Applicants further amended Claim 1 so that step (iv) reads "dissolving the chloroform extract as obtained in step (iii) in methanol followed by chromatographic separation to obtain withaferin-A."

With respect to the rejection of Claim 2, Applicants amended the claim to read, in part, "varying in the range of less than 100 % to greater than 0 %."

Applicants also made minor amendments to dependent claims 3-4 and 7-15 so that those claims are in a more conventional U.S. Patent format.

In view of the foregoing amendments, Applicants respectfully request reconsideration and withdrawal of the § 112, second paragraph, rejections.

Claims 1-17 stand provisionally rejected under 35 U.S.C. § 101 as claiming same invention claimed in co-pending Application Serial No. 10/812,363. Because the '363 application has been or will soon be abandoned, the double patenting rejection over the '363 application is moot.

Applicants respectfully request reconsideration and withdrawal of the double patenting rejection over the '363 application upon abandonment of the '363 application.

Claims 1-17 stand rejected under 35 U.S.C. § 103(a) over Nair (U.S. Patent Published Application No. 2004/0096524) and Dinan (J. Chromotogr. A, 2001) in view of Kaufmann (Chromatographia, 2001). For at least the reasons that follow, withdrawal of the rejection is in order.

Independent Claim 1 recites an improved process for isolation of withaferin-A from plant materials, said process comprising the steps of:

- (i) extracting the plant materials in an aqueous alcohol extraction solvent,
- (ii) defatting the extract, as obtained in step (i), with partitioning with n-hexane followed by chromatographic separation to obtain a withanolide preparation,
- (iii) portioning out withanolide aglycones from the withanolide preparation, as obtained in step (ii), into chloroform followed by evaporation of said chloroform to obtain a chloroform extract, and
- (iv) dissolving the chloroform extract as obtained in step (iii) in methanol followed by chromatographic separation to obtain withaferin-A. (Emphasis added.)

In order to establish a *prima facie* case of obviousness, the prior art references (or references when combined) must teach or suggest all of the claim features. See In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In addition, "all words in a claim must be considered in judging the patentability of that claim against the prior art." See In re Wilson, 424 F.2d 1382, 1385; 165 U.S.P.Q. 494, 496 (CCPA 1970). See MPEP § 2143.03.

The Official Action asserts that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate/provide withaferin-A by the steps claimed. (See Official Action at page 8.) Applicants respectfully disagree.

First, Nair is directed to the COX-2 inhibitory activity of withanolides from *Withania somnifera*. The isolation process Nair discloses is for withanolides and glycol-withanolides, not for withaferin-A. In fact, the process of Nair is substantially

different from the claimed process. Specifically, the extraction process in Nair is sequential (i.e., a process of steps performed in one-by-one succession). The process includes: (1) using dichloromethane and methanol in a 1:1 ratio; (2) then using methanol alone; (3) then using water alone; and (4) then combining the three extracts. (See, for example, Nair at page 5, paragraph 46). In stark contrast, the process of Claim 1 employs an aqueous-alcohol extraction solvent. Thus, unlike Nair, the process of Claim 1 uses alcohol and water together; it does not use methanol and water by themselves in two separate steps performed in the sequence described in Nair.

In addition, dependent Claims 4 and 9 specify that the extraction solvent is 40% water and 60% alcohol, and dependent Claim 14 specifies that the extraction is performed using fresh herbs. Nowhere does Nair disclose or suggest performing an extraction using a 40 : 60 (water : alcohol) extraction solvent or performing an extraction using fresh herbs to provide a withaferin-A yield greater than that obtained using dried herbs. In fact, Nair specifically discloses obtaining an extract from a third party or using shade dried leaves instead of fresh leaves. For at least these reasons, dependent Claims 4, 9 and 14 are also patentable over Nair.

Dinan does not overcome the deficiencies of Nair.

Dinan is an article about steroids and discusses withanolides as a class and merely provides a structure of withaferin-A in Fig. 1. Dinan describes extraction of plant material in methanol or ethanol. The discussion in Dinan of subsequent mixing in water is conducted solely to remove pigment. Nowhere does Dinan disclose or fairly suggest extracting withaferin-A using an aqueous alcohol extraction solvent, as specified in Claim 1. That is, Dinan only discloses use of a 100% methanol or

ethanol extraction solvent and subsequent mixing with water to remove pigment. In addition, concerning dependent Claims 4, 9 and 14, nowhere does Dinan disclose or fairly suggest using an extraction solvent having a water to alcohol ratio of 40:60 or performing an extraction of withaferin-A using fresh herbs to obtain a greater yield.

Kaufmann fails to overcome the deficiencies of Nair and Dinan, taken alone or in combination. Kaufmann relates to isolation of withanolides from dried plant material using a mechanical process called Pressurized Solvent Extraction (PSE) wherein matrix analyte interactions occur. The study discussed in Kaufmann is directed to extraction of iochromolide, not an extraction of withaferin-A. In Kaufmann, the extractant used is a water: methanol extractant having a 1:1 ratio provided at a flow rate of 0.5%, which was found to provide a better PSE parameter than when using methanol or methanol and water in a ratio of 8:2 of dry *lochroma* plant. (See, Kaufmann, for example, at Fig. 4.)

The process of Claim 1 is directed to the extraction of withaferin-A not iochromolide. It is well known that the extractability of each withanolide is quite different. These extractability characteristics can be seen, for example, from Fig. 1 of Applicants' application. Kaufmann only discloses using a 1:1 water: methanol extractant at a flow rate of 0.5% to obtain a desired PSE parameter for extraction of iochromolide. There is no disclosure or suggestion in Kaufmann of performing an isolation of withaferin-A using an aqueous alcohol extract, as claimed in claim 1. Furthermore, there is no disclosure or suggestion of isolating withaferin-A using a 40 : 60 (water : alcohol) extractant or fresh herbs, as further specified in dependent claims 4, 9 and 14, respectively.

Thus, a *prima facie* case of obviousness cannot be established over the above-asserted combination of references because none of the references, alone or in combination teach or suggest all of the features of Claim 1. Specifically, none of the references alone or in combination, teaches or suggests a process for isolation of withaferin-A from plant materials comprising extracting the plant materials in an aqueous alcohol extraction solvent, as specified in Claim 1. Furthermore, a rejection based on the asserted combination of references does not reflect a proper consideration of all words in Claim 1 (as amended) in judging the patentability of that claim against the cited references. Thus, a *prima facie* case of obviousness cannot be established over the asserted combination of references for at least this additional reason.

For at least the above reasons, Claim 1 is patentable over the asserted combination of Nair, Dinan and Kaufmann. Because the remaining claims (Claims 2-15) depend, directly or indirectly, from independent Claim 1, these claims are also patentable over the asserted combination of references for at least the reasons that Claim 1 is patentable. Applicants respectfully request reconsideration and withdrawal of the § 103 rejection.

From the foregoing, Applicants earnestly solicit further and favorable action in the form of a Notice of Allowance.

If there are any questions concerning this paper or the application in general,
Applicants invite the Examiner to telephone the undersigned at the Examiner's
earliest convenience.

Respectfully submitted,

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